



## The Metabolism of Liver Cancer Treatment Drug Sorafenib is Affected by Acetaminophen Treatment

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**SUMMARY.** Sorafenib is a commonly used drug for the treatment of liver cancer, and sorafenib has high possibility to co-administration with acetaminophen (APAP) which has been frequently used in the clinic. The present study aims to evaluate the metabolic behavior in acetaminophen-treated mice. Intraperitoneal injection with 500 mg/kg body weight of APAP was employed to induce the liver damage. The results showed APAP treatment resulted in the alter histology of liver, and increased activity of aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Western blotting analysis showed that APAP treatment can decrease the expression of drug-metabolizing enzymes cytochrome P450 (CYP) 3A4 and UDP-glucuronosyltransferase (UGT) 1A9, which furtherly weakened the oxidation and glucuronidation metabolism of sorafenib. In conclusion, the metabolism of sorafenib was significantly decreased in acetaminophen-treated mice, which guiding the clinical application of acetaminophen and sorafenib.

**RESUMEN.** Sorafenib es un medicamento utilizado comúnmente para el tratamiento de cáncer de hígado que tiene una alta posibilidad de co-administración con acetaminofeno (APAP), combinación utilizada con frecuencia en la clínica. El presente estudio tiene como objetivo evaluar el comportamiento metabólico en ratones tratados con paracetamol. Se empleó una inyección intraperitoneal de APAP de 500 mg/kg de peso corporal para inducir el daño hepático. Los resultados mostraron que el tratamiento APAP alteró la histología de hígado, con aumento de la actividad de la aspartato aminotransferasa (AST) y la alanina aminotransferasa (ALT). El análisis por Western blot demostró que el tratamiento con APAP puede disminuir la expresión de las enzimas metabolizadoras de fármacos del citocromo P450 (CYP) 3A4 y UDP-glucuronosiltransferasa (UGT) 1A9, lo que posteriormente debilitó el metabolismo de oxidación y glucuronidación de sorafenib. En conclusión, el metabolismo de sorafenib se redujo significativamente en los ratones tratados con paracetamol, hecho que debe guiar la aplicación clínica de acetaminofeno y sorafenib.

**KEY WORDS:** acetaminophen, drug-drug interaction, liver cancer, sorafenib

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